

## **REMARKS**

Claim 1 has been canceled and claims 2, 14, and 15 have been amended to more particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The amendments are fully supported in the specification as filed. Claims 3-13 and 17-27 are withdrawn from consideration. Claims 2, 14, 15, and 16 are pending.

### **1. The Rejections Under 35 U.S.C. 112, First Paragraph Are Obviated**

Claims 1-2 and 14-16 are rejected under 35 U.S.C., first paragraph, for lack of enablement. Claims 1-2 and 14-16 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Applicant respectfully disagree with the rejections.

In response, without acquiescing to the propriety of the rejections, and solely to advance prosecution and obtain coverage for certain embodiments of the invention, Applicant has canceled claim 1 and amended claim 2 to recite a protein consisting of the amino acid sequence of SEQ ID NO: 24.

In the office action, the Examiner acknowledges that the specification is enabling for a polypeptide consisting of SEQ ID Nos: 6, 10, 12, 18 or 24 which has deposition activity onto extracellular matrix, or a fusion protein comprising a polypeptide consisting of SEQ ID NOs: 6, 8, 10, 12, 18 or 24 linked to a molecule of interest to be expressed. The Examiner also acknowledges that Applicant is in possession of a polypeptide consisting of SEQ ID NOs: 6, 8, 10, 12, 18 or 24 which has deposition activity onto extracellular matrix, or a fusion protein comprising a polypeptide consisting of SEQ ID NOs: 6, 8, 10, 12, 18 or 24. As such, claim 2 and its dependent claims 14, 15 and 16 meet the requirements of 35 USC 112, first paragraph.

With respect to the drug delivery system of claim 16, Applicant points out that it is now based on using the protein of claim 2 that is clearly defined by its structure and biochemical properties. As demonstrated in the examples, a fusion protein comprising the amino acid sequence of SEQ ID NO: 24 and alkaline phosphatase has enabled the delivery of an enzyme to the extracellular matrix (ECM), and the alkaline phosphatase retained its

enzymatic activity towards the chromogenic substrate, BCIG (see Fig. 1). In the rejection, the examiner has not provided any reason or evidence that the results obtained *in vitro* cannot be obtained with the claimed fusion protein *in vivo*. The examiner merely alleged that there is a lack of predictability in the art and a lack of established clinical protocol. A patent applicant's specification which contains a teaching of how to make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *In re Marzocchi*, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971); *In re Brana*, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995). The examiner bears the initial burden of asserting reasons for such doubt credible to one of skill in the art. Furthermore, Applicant respectfully points out that many prodrugs that require enzymatic activation at their therapeutic target *in vivo* were tested clinically with well established protocols and received regulatory approval. Thus, any experimentation needed to practice the claimed invention in a given situation would not be undue, but rather would lie well within the ability of one of ordinary skill in the art. Given that the skill in the art was quite high and applicable clinical protocols are well known, a conclusion of enablement should be made.

In view of the foregoing, the rejections are obviated and Applicant respectfully requests withdrawal of the rejections.

## **2. The Rejections Under 35 U.S.C. 102 Are Obviated**

Claims 1-2 and 14-16 are rejected under 35 USC 102 as being anticipated by US Patent 6,812,339 (the '339 patent). The Examiner alleges that the '339 patent teaches a 448-amino acid protein (SEQ ID NO: 10130) which comprises the amino acid sequence of SEQ ID NO: 24 at positions 91-316.

Claims 1-2 and 14-16 are also rejected under 35 USC 102 as being anticipated by US Patent 5,874,562 (the '562 patent). Allegedly, the '562 patent teaches (i) a 513-amino acid protein comprising the claimed SEQ ID NO: 24, at positions 155-381 and has two substitutions (P92K and S123F) and a single addition (R between amino acids 92 and 93); (ii) a polypeptide of 460 amino acids comprising the amino acid sequence of SEQ ID NO: 14 from residue #54 through #51, which comprises SEQ ID NO: 24 of the present invention, with substitutions and addition as above; and (iii) a 321-amino acid protein comprising the

amino acid sequence of SEQ ID NO: 24 except the 35 amino acids at the N-terminal, and further substitutions and additions.

Claims 1-2 and 14-16 are also rejected under 35 USC 102 as being anticipated by US Patent 5,887,281 (the '281 patent). Allegedly, the '281 patent claims a polypeptide comprising three epidermal growth factor-like domains and two discoidin I/factor VIII-like domains contained within the amino acid sequence as shown in patented SEQ ID NO: 24 (at positions 155-381) with two substitutions (P92K and S513F) and a single addition (R between positions 92 and 93) of SEQ ID NO: 24 of the present invention; (ii) a 321-amino acid protein comprising the amino acid sequence of SEQ ID NO: 24 except the 35 amino acids at the N-terminal, and further substitutions and additions.

The legal standard for anticipation is well recognized. The Court of Appeals for the Federal Circuit ("CAFC") in Scripps Clinic & Research Foundation v. Genentech, Inc., 927 F.2d 1565 (Fed. Cir. 1991) made it absolutely clear that "anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference ... [and] ... [t]here must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." Scripps v. Genentech, 927 F.2d at 1576.

Applicant submits that amended claim 2 is directed to a protein consisting of the amino acid sequence of SEQ ID NO: 24 that has 226 amino acid residues. None of the references cited by the Examiner discloses a protein that has 226 amino acid residues identical to SEQ ID NO: 24, or a fusion protein with this sequence of 226 amino acids. The proteins in the references cited by the examiner are contiguous, and larger and/or contain substitutions, deletions, and/or additions of amino acid residues, relative to SEQ ID NO: 24. As such, the proteins disclosed in the references are not identical to, and thus do not anticipate, the claimed invention.


In view of the foregoing, the rejections are obviated and Applicant respectfully requests withdrawal of the rejections.

**CONCLUSION**

Applicant respectfully requests that the above-made amendments and remarks be entered and made of record in the instant application. An early allowance is earnestly requested.

Respectfully submitted,

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Enclosure